CERTIFICATE OF TRANSMISSION BY FACSIMILE (37 CFR 1.8) Applicant(s): KESSLER, S., ET AL			Docket No. 1951
Application No. 10/030,278	Filing Date 04/09/2002	Examiner HOWARD, S.	Group Art Unit 1951

Invention: **PRESERVATIVE FOR PERISHABLE PREPARATIONS...**

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Examiner: S. L. Howard; Art Unit: 1615; Docket No.: 1951

In RE: **Application of Susanne KESSLER, et al**

Ser. No.: **10/030,278**

Filing Date: **April 9, 2002**

November 11, 2004

DECLARATION OF FACTS FILED UNDER 37 C.F.R. 1.132 TO OVERCOME REJECTIONS UNDER 35 U.S.C. 103 (a)

Hon. Commissioner of Patents
and Trademarks,
Washington, D.C. 20231

Sir:

In response to the Office Action dated July 14, 2004 and in addition to the accompanying amendment filed under 37 C.F.R. 1.114, please accept the following showing of experimental facts supporting the claims of the above-identified U.S. Patent Application:

WHEREAS WE, Susanne **KESSLER** and Sean **LEE**, citizens of Germany, whose post office addresses and residences are, respectively, Johannisweg 23, 84030 Ergolding, Germany; and Oberlinstrasse 17, 76227 Karlsruhe, Germany; have applied for Letters Patent for a new and improved

PRESERVATIVE FOR PERISHABLE PREPARATIONS PARTICULARLY FOR COSMETIC AND PHARMACEUTICAL FORMULATIONS

in a U.S. Patent Application, Ser. No. 10/030,278, filed April 9, 2002, of which claims 10 to 20 have been rejected under 35 U.S.C. 103 (a) in a final Official Action dated July 14, 2004 over the article by J. Allen, "Antibacterial Properties of a Bioactive Glass".

WHEREAS WE have tested aqueous compositions containing 1 percent by weight of bioactive glass particles of various particle sizes in a range from 1 to 10 µm and have found that the pH unexpectedly and surprisingly depends on the particle size becoming smaller as the particle size decreases in a particle size range from 1 to 10 µm.

WHEREAS WE have tested aqueous compositions containing 1 percent by weight of bioactive glass particles in a particle size range from 1 to 10 µm and have found surprisingly that the smaller particle sizes are unexpectedly and surprisingly more effective in preventing bacterial growth of some bacteria, especially *Candida albicans* and *Aspergillus Niger*, in these aqueous compositions.

I. TEST METHODS

Solutions of bioactive glass particles of different particle sizes in aqueous media were prepared. The ability of the bioactive glass particles to prevent growth of various bacteria in the aqueous media was tested. Standard growth inhibition test methods were used. Each different solution contained 1 % by weight of bioactive glass particles with a correspondingly different particle size in a range from 1 to 10 μm. Each different solution was inoculated at the start of the test with a cocktail containing a mixture of known common bacteria in known amounts. The mixture of bacterial species included *Escherichia Coli, Pseudomonas aeruginosa, Staphylococcus aureus, Candidia albicans and Aspergillus Niger*. The amounts of the respective bacteria present at certain fixed time intervals were measured by standard test methods.

The bioactive glass particles had a standard composition, designated MD01, which is a preferred composition for bioactive glass used in the present application. The composition is given in Table I below.

TABLE I. Bioactive Glass Composition

	MD01
SiO_2	45.00
Na_2O	24.00
CaO	24.50
P_2O_5	**6.00**
Al_2O_3	-
MgO	-

Various particles sizes of MD01 were employed in preparing the different preparations. It was found that the pH in the various aqueous preparations became more basic as the particle size decreased in a range from 1 to 10 μm. The following Table II shows the pH at 15 min and 24 h after preparation of these compositions.

TABLE II. pH of Aqueous Preparations of MD01 Bioactive Glass Particles

Particle Size, μm	pH at t = 15 min	pH at t = 24 h
1.6	11.23	11.38
1.9	11.2	11.33
3.5	10.99	11.18
4	10.71	10.96
9	10.56	10.85

Of course it would make some sense if it could be shown that bacterial growth is inhibited when the preparation is more alkaline.

II. BACTERIAL GROWTH INHIBITION TEST RESULTS

The following two tables show the test results for the above-described bacterial growth inhibition tests for a 1 % preparation of MD01 bioactive glass particles having a 4 μm particle size (TABLE III) and for a 1 % preparation of MD01 bioactive glass particles having a 2 μm particles size (TABLE IV).

The tables show the number of surviving bacteria species of a particular type as measured at a certain number of days after the initial inoculation of the solutions with the mixture of the various listed bacteria.

TABLE III. BACTERIAL COUNTS IN AN AQUEOUS SOLUTION OF MD01 PARTICLES OF 4 μm PARTICLE SIZE

DAYS AFTER INNOCULATION

Species	0	2	7	14	21	28
E. Coli	250000	0	0	0	0	0
P. aeruginosa	350000	0	0	0	0	0
S. aureus	270000	0	0	0	0	0
C. albicans	300000	1800	0	0	0	0
A. Niger	250000	200000	100000	40000	40000	28000

TABLE IV. BACTERIAL COUNTS IN AN AQUEOUS SOLUTION OF MD01 PARTICLES OF 2 μm PARTICLE SIZE

DAYS AFTER INNOCULATION

Species	0	2	7	14	21	28
E. Coli	250000	0	0	0	0	0
P. aeruginosa	350000	0	0	0	0	0
S. aureus	270000	0	0	0	0	0
C. albicans	300000	<100	0	0	0	0
A. Niger	250000	20000	6000	300	300	200

III. CONCLUSIONS

The bacterial inhibition test results in tables III and IV show that the bioactive glass particles, which are smaller in size, namely the particles with an average diameter d_{50} of 2 μm, were surprisingly and unexpectedly more effective inhibiting bacterial growth of some of the bacterial species. This effect was most pronounced for *A. Niger*, but also was observed for *C. Albicans*.

These results clearly show that the finest particles sizes for the bioactive glass particles are more universally inhibiting of bacterial growth of a wide variety of bacterial species and thus unexpectedly better than the larger particle sizes, such as those used by J. Allen (see page 2, first paragraph, of the English translation of the specification). The current obviousness rejection of pending claims in this application is based on the J. Allen article, which describes bacterial inhibition experiments using bioactive glass having particle sizes of 355 to 500 μm, which of course are much larger. Applicants' experimental results above suggest that bioactive glass with these larger particles sizes would not be immediately effective against contamination by *A. Niger* or else much larger amounts of the bioactive glass would be necessary.

Also it is well to remember that a claimed composition need only be unexpectedly better than the prior art with respect to a single property (M.P.E.P. 716.02 (a) I and II) to overcome a case of *prima facie* obviousness under 35

U.S.C. 103 (a). In the case of the instant application that single property is inhibition of growth of *A. Niger* (possibly also *C. albicans*).

In summary, the bacterial inhibition results shown in Tables III and IV above clearly show that the finest bioactive glass particles sizes below 10 μm are surprisingly and unexpectedly more effective in inhibition of growth of at least some bacterial species.

WE HEREBY DECLARE AND AFFIRM THAT ALL STATEMENTS made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statement may jeopardize the validity of the above-named application, any patent issuing thereon or any patent to which this Declaration is directed.

18. Nov. 2004 — Susanne Kessler

DATE — Sussane KESSLER

DATE — Sean LEE

WE HEREBY DECLARE AND AFFIRM THAT ALL STATEMENTS made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statement may jeopardize the validity of the above-named application, any patent issuing thereon or any patent to which this Declaration is directed.

DATE	Sussane KESSLER
22.10.09	
DATE	Sean LEE